IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of:
Holman

Application No.: 10/582,422 | Confirmation No.: 4848

Filed: June 9, 2006 | Art Unit: 3768

For: CATHETER-BASED MID-INFRARED REFLECTANCE AND REFLECTANCE GENERATED ABSORPTION SPECTROSCOPY | Examiner: J. F. Brutus

SUPPLEMENTAL AMENDMENT UNDER RULE 111

This correspondence is being filed electronically and is addressed to: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450 on the date shown below:

Eileen Sheffield — Date: April 11, 2011

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

Responsive to the non-final office action mailed August 24, 2010, and supplemental to the response filed on February 18, 2011, please amend the above-identified patent application as follows:

IN THE CLAIMS

Claims 1-28 (canceled)

29. (currently amended) A method of characterizing conditions in a tissue, comprising (a) providing a catheter that has a light source that emits light in the mid-IR spectrum range of 4000 – 400 cm^{-1} wavenumber ~~selected wavenumbers within the range of mid-IR spectrum~~; (b) directing the light from the catheter to an area of tissue at a location inside a blood vessel of a subject; (c) collecting light reflected from the location and generating a reflectance spectra; and (d) comparing said reflectance spectra to a reference spectra of normal tissue, whereby a location having an increased number of absorbance peaks at said selected wavenumbers indicates a tissue inside said blood vessel containing a physiological marker for atherosclerosis, wherein the comparing step comprises that increased numbers of absorbance peaks at said selected wavenumbers are within at least one range of mid-infrared wavenumbers selected from the group of: about 3500-3000, about 3020-3000, about 2950-2800, about 1800-1450, about 1710-1760, about 1690-1610, about 1520-1500, about 1480-1450, about 1100-900 and about 900-400 cm^{-1}.

30. (currently amended) A method of characterizing conditions in a tissue, comprising (a) providing a catheter that has a light source that emits light in the mid-IR spectrum range of 4000 – 400 cm^{-1} wavenumber ~~selected wavenumbers within the range of mid-IR spectrum~~; (b) directing the light from the catheter to an area of tissue at a location inside a blood vessel of a subject; (c) collecting light reflected from the location and generating a reflectance spectra; and (d) comparing said reflectance spectra to a reference spectra of normal tissue, whereby a location having an increased number of absorbance peaks at said selected wavenumbers indicates a tissue inside said blood vessel containing a physiological marker for atherosclerosis, wherein the comparing step comprises that increased numbers of absorbance peaks at said selected wavenumbers is in the range of wavenumbers 4000 to 400 cm^{-1}.

31. (canceled)

32. (previously presented)The method of claim 29 wherein the comparing step comprises that increased numbers of absorbance peaks at said selected wavenumbers are in the range between about 3000-3100 cm^{-1} and between about 1710-1760 cm^{-1}.

33. (previously presented)The method of claim 29, further comprising the step of generating a spatially resolved map of reflectance generated spectral signals from different locations within a single vessel.

34. (currently amended) An apparatus for characterizing tissue conditions, comprising: (a) a single or multiple source of mid-IR light that emits light in the mid-IR spectrum range of 4000 – 400 cm^{-1} wavenumber ~~covering a range of mid-infrared wavenumbers~~; (b) a catheter coupled to said source and a detector to detect light reflected by tissue of a blood vessel of a subject; (c) a computer means for generating the reflectance generated spectra at selected wavenumbers detected by said detectors and containing the generated spectra to a reference spectra of normal tissue, to determine whether the subject has atherosclerosis.

35. (previously presented)The apparatus of claim 34, wherein said computer means has stored therein the reference wavenumber range of 4000 to 400 $cm.^{1}$.

36. (previously presented)The apparatus of claim 35, wherein said computer means has stored therein at least one of the following reference wavenumber ranges, expressed in cm^{-1}: about 4000-2800, about 3500-3000, about 3020-3000, about 2950-2800, about 1760-1710, about 1690-1610, about 1520-1500, about 1480-1450, and about 1100-900 and about 900-400.

37. (previously presented)The apparatus of claim 34, further comprising an interferometer.

38. (previously presented)The apparatus of claim 34, wherein said catheter comprises a source fiber and a detection fiber having a tip or a tip array.

39. (previously presented)The apparatus of claim 34, further comprising a tuning system for said source.

40. (previously presented)The apparatus of claim 34, further comprising a cooling means for said detector.

41. (previously presented)The apparatus of claim 40, further comprising the additional use of customized bandwidth and special gain for DC- and/or AC-coupled preamps for the detectors to increase the signal-to-noise ratio of the detectors.

42. (previously presented)A method of characterizing atherosclerotic material that has enhanced reflectance and/or spectral features, comprising the steps of: (a) providing light in selected mid-IR wavenumbers between about 4000 to about 400 cm^{-1}; (b) directing the light

through a probe to an area of said biological material; (c) measuring reflected light returning through the probe over a range of said wavenumbers to generate a pattern of spectral signals representative of said area; and (d) comparing spectral signals from a reference spectra to the spectral signals from said area for enhanced reflectance and/or spectral features.

43. (currently amended) A method of spectroscopic diagnosis of tissue comprising: irradiating a subsurface portion of tissue at a target area in the blood vessel of a subject with radiation having a frequency within the mid-infrared range of 4000 – 400 cm^{-1} wavenumber, transmitted through a fiber optic cable; detecting light reflected by the area of tissue in response to the radiation, the light having a range of 4000 cm^{-1} to 400 cm^{-1}; and analyzing the detected reflectance light to diagnose whether the tissue is atherosclerotic including the step of comparing the detected light with reference data.

44. (previously presented)The method of claim 43, wherein the detecting step further comprises collecting the reflected light through the fiber optic cable.

45. (previously presented)The method of claim 43, wherein the irradiation step further comprises a catheter means for insertion of the fiber optic cable in body lumens.

46. (previously presented)The method of claim 43, wherein the fiber optic cable receives light reflected by the tissue and transmits the reflected light to a spectroscopic analysis system.

47. (previously presented)The method of claim 43, further comprising an alternate spectrophotometer to receive the reflected light.

48. (previously presented)The method of claim 43, further comprising the step of rotating the fiber optic cable radially within the blood vessel, whereby data is acquired at various target locations radially within the lumen.

49. (previously presented)The method of claim 48, wherein the steps are repeated thereby performing a 360-degree spectral analysis of the body lumens.

50. (currently amended) A method of detecting atherosclerotic conditions in a blood vessel tissue of a subject comprising the steps of: delivering mid-infrared light in the range of 4000 – 400 cm^{-1} wavenumber to a tissue to be diagnosed, irradiating said blood vessel tissue with said light, detecting any delivered light reflected by any atherosclerotic tissue within the same

range as the mid-infrared delivered light, and determining the chemical composition and cellular conditions in atherosclerotic tissues.

REMARKS

Entry of this amendment, and reconsideration of this application, as amendment, are respectfully requested.

The undersigned gratefully acknowledges the courtesies extended by the Examiner during the telephone interview of March 21, 2011.

Claims have been amended to incorporate the limitation that a light source emits light in the range of 4000 – 400 cm^{-1} wavenumber. Support for these amendments can be found, for example, at page 6-7, paragraph [021]. No new matter has been introduced.

Please note that wavenumber means $1/\lambda$ where λ represents the wavelength. Wavenumber and wavelength can be inter-converted using the equation set forth in page 12, paragraph [045] of the specification. For example, wavenumber 4000 – 400 cm^{-1} can be converted to 2.5 – 25.0 μm wavelength.

Claims 29-40 and 42-50 were rejected under 35 U.S.C. §103(a) over Alfano in view of Dukor. Claim 41 was rejected under 35 U.S.C. §103(a) over the Alfano, Dukor and Corenman. Applicants respectfully traverse each of these rejections.

The presently claimed invention discloses methods and apparatus for *in vivo* detecting and characterizing conditions in abnormal tissues that present in vascular diseases, in particular, atherosclerosis, by using reflection-based mid-infrared (IR) spectroscopy. Specifically, the presently claimed invention teaches the use of a light source emitting light in the range of about 4000 to 400 cm^{-1} wavenumber or 2.5-25 μm wavelength. This feature is set forth in the amended claims.

Alfano fails to teach or suggest a light source emitting light in the range set forth in the present invention. In contrast, Alfano discloses a light source capable of emitting light at about 680-1350 nm (equivalent to 0.68 μm-1.35 μm), see, col. 4, line 61 of Alfano, which is outside the range claimed in the present invention, which is 2.5 – 25.0 μm wavelength as mentioned above.

Moreover, the presently claimed invention teaches the use of signature mid-IR spectral bands as diagnostic marker for atherosclerotic disease. Those signature bands are set forth in claim 29.

Applicants reiterates that Alfano fails to teach or suggest the use of claimed signature mid-IR spectral bands to diagnose atherosclerosis. The Examiner alleges that Alfano discloses the wavenumbers 1659 cm^{-1} and 957 cm^{-1}, which fall within the claimed mid-IR spectral band range. Applicants respectfully submit that the Examiner misinterprets Alfano.

In the presently claimed invention, those signature bands are from reflectance spectra. In abnormal tissues, increased absorbance peaks at those selected wavenumbers are observed. In contrast, the wavenumbers 1659 cm^{-1} and 957 cm^{-1} described by Alfano are not from reflectance spectra, but are Raman bands at Raman Shifts. Raman Shifts don't refer to absorbance peaks at specific wavenumbers at all, but are indicators of light shift, i.e., the difference between wavenumbers. See, for example, col. 7, line 68-col. 8, line 13 ("...v_1 and v_2 are the wavenumbers of two different Raman shifts....one can determine if a human aortic tissue sample is calcified atherosclerotic tissue either by noting the presence of light shifted by 957 cm^{-1}...). Furthermore, the formula to calculate Raman shift is

$$\Delta w = \left(\frac{1}{\lambda_0} - \frac{1}{\lambda_1}\right)$$

, where Δw is the Raman shift expressed in wavenumber, $\lambda 0$ is the excitation wavelength, and $\lambda 1$ is the Raman spectrum wavelength. (See http://en.wikipedia.org/wiki/Raman_spectroscopy).

As explained above, although Raman shift is expressed in the format of a wavenumber, it does not refer to reflectance or absorption at a specific wavenumber at all. Therefore, the wavenumbers 1659 cm^{-1} and 957 cm^{-1} described by Alfano have entirely different meanings from the wavenumbers claimed in the present invention. Thus, Alfano does not teach or suggest the use of the claimed signature mid-IR spectral bands to diagnose atherosclerosis at all.

The deficiencies of Alfano are not overcome by either Dukor or Corenman.

Furthermore, applicants would like to emphasize that as explained in previously submitted Rule 132 declaration of inventor Hoi-Ying Holman, Dukor merely discloses a method and system for diagnosing carcinoma by using IR spectroscopy, NOT reflective IR spectroscopy as in the presently claimed invention. In addition, Dukor does not teach or suggest using the reflective IR spectroscopy technique to diagnose atherosclerosis. Due to the huge difference between carcinoma tissue and atherosclerosis tissue, the reflective IR spectroscopy as in the

presently claimed invention can't be applied to carcinoma diagnosis. Thus, a skilled artisan would not have combined Alfano and Dukor to arrive at the present invention.

Therefore, all §103(a) rejections should be withdrawn.

In view of the foregoing allowance is respectfully requested.

The Commissioner is hereby authorized to charge any deficiency in the fees filed, asserted to be filed or which should have been filed herewith (or with any paper hereafter filed in this application by this firm) to our Deposit Account No. 50-0624, under Order No. NY-LBNL-238-US.

Respectfully submitted

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